Abstract

The role of glutamate transporter GLT-1 in memory and long-term potentiation (LTP) of hippocampal dentate gyrus neurons in an okadaic acid-induced model of Alzheimer's disease

Background: Alzheimer's disease (AD) is a neurodegenerative disorder with a progressive cognitive decline and memory loss. Multiple pathological factors including aggregated β-amyloid (Aβ), intracellular neurofibrillary tangles (NFTs) and oxidative stress are involved in AD. Okadaic acid (OKA), a selective and potent inhibitor of the serine/threonine (Ser/Thr) phosphatases 1 and 2A induces hyperphosphorylation of tau protein which resembles the Alzheimer's disease (AD) pathology. In the present study we examined the protective effect of ceftriaxone, as up-regulator of GLT-1 expression on learning, memory and long-term potentiation (LTP) in hippocampal DG neurons.

Methods: Male Wistar rats were divided into five groups including control, OKA, ceftriaxone, ceftriaxone + OKA and ceftriaxone + OKA + DHK groups. OKA was injected intracerebroventricularly (i.c.v.) into lateral ventricles and after two weeks the behavioral and electophysiological tests performed to determine long term potentiation (LTP) in hippocampal DG neurons.

Results: Administration of OKA drastically attenuated the learning and memory, while there was no significant difference in control and ceftriaxone groups. Electrophysiological and immunohistochemistry observations showed a significant difference between the groups. Administration of ceftriaxone had improving effect on OKA-induced impairment in memory and elcerophysiological responses.

Conclusions: This study revealed protective effects of GLT-1 over-expression by ceftriaxone on the synaptic failure induced by OKA and has introduced this transporter as a possible pharmacological agent in treatment of AD in the future.

Keywords: Alzheimer's disease, β-amyloid peptide, GLT1, Long term potentiation.